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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,014	06/06/2006	Shuchong Pan	07039-409US1	9426

26191 7590 09/05/2008

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EXAMINER	
WANG, CHANG YU	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
09/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,014	PAN ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *11-15, 17-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/16/05* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/31/06,11/07/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Election/Restrictions

1. Applicant's election without traverse of Group III (claims 1-10, 16, 18, 19), SEQ ID NO:3 in the reply filed on 5/15/08 is acknowledged.

Claims 1-44 are pending. Claims 11-15, 17, 20-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. In addition, claims 18 and 19 are also withdrawn from consideration because of non-elected sequences. Election was made **without** traverse in the reply filed on 5/15/08. Although SEQ ID NOs: 1 and 36 are not elected SEQ ID NO., SEQ ID NOs:1 and 36 are part of the C-terminus of the amino acid sequence of SEQ ID NO:3 (elected sequence), the restriction on SEQ ID NOs: 1, 36 will be withdrawn and will be included and under examination in this office. Claims 1-10 and 16 are under examination with respect to SEQ ID NOs:1, 3 and 36 in this office action.

Drawings

2. The drawings/figures 1, 2 and 4 are objected to because the sequence listings included in the specification must not be duplicated in the drawings. See 37 C.F.R. §1.58(a) and §1.83. Appropriate correction is required.

Specification

3. The use of the trademark (see p.12, p.21, p.26-28, p.30, p. 34) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

4. Claims 1-10 and 16 are objected to as encompassing non-elected sequences.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for a purified polypeptide BNP2 comprising the amino acid sequence of SEQ ID NO: 3, does not reasonably provide enablement for a structurally and functionally polypeptide comprising SEQ ID NO:1 and 36 and their variants at least 65% to a fragment of SEQ ID NO:1 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in the scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to: (A) The breadth of the claims;(B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Breadth of the claims: Claims 1-10, and 16 are drawn to an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:3, SEQ ID NO:1, SEQ ID NO:36 or a sequence having at least 65% identity to a fragment of SEQ ID NO:1. The claims encompass a genus of polypeptides comprising structurally and functionally undefined fragments and their variants derived from the above recited SEQ ID NOs.

Nature of the invention: The instant invention identifies different alternative splicing isoforms of brain natriuretic peptide (BNP). The increased level of BNP can be detected in patients with congestive heart failure and has been used as a diagnostic marker for detection heart failure. The specification teaches that the full-length amino acid sequence of human BNP2 is set forth in SEQ ID NO:3 and the sequence of the mature BNP2 polypeptide is set forth in SEQ ID NO:36. The specification teaches

detection of an increased level of BNP2 in heart tissue from patients suffering from heart failure using an antibody raised against to the residues 27-60 of the mature human BNP2. The specification also teaches that the RNA expression level of BNP2 in patients with heart failure is 7 times higher than the level in normal controls.

State of the prior art/predictability/experimentation: Based on the specification, Applicant is enabled for a purified polypeptide comprising the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:36. The claims are not limited to the polypeptides as set forth above. The claims encompass a genus of polypeptides comprising structurally and functionally undefined fragments and variants derived from SEQ ID NOs:1, 3 and 36. Although the function and activity of the peptides of SEQ ID NOs: 3 and 36 are known based on the disclosure of the instant specification, the specification fails to teach what the function and activity of SEQ ID NO:1 are. Although SEQ ID NO:1 is part of SEQ ID NO:3, the specification fails to teach how to make and use the peptide of SEQ ID NO:1. Thus, the polypeptides comprising structurally and functionally undefined sequences derived from SEQ ID NO:1 are also not enabled because the function and activity of SEQ ID NO:1 and their variants are unknown.

The specification fails to provide sufficient guidance as to what common sequences, structures and characteristics are required for the fragments and variants derived from SEQ ID NOs:1, 3, and 36 as encompassed by the instant claims. There is no guidance as to what can or cannot be changed or included in order to preserve the activity or function or characteristics of the peptides of SEQ ID NO: 3 and 36. In addition, there is no particular activity required for these claimed variant polypeptides

and fragments with limited homology to SEQ ID NO:1. Furthermore, the specification provides insufficient guidance as to how to make and use this broad genus of polypeptide comprising structurally and functionally undefined fragments and variants derived from SEQ ID NO:1, 3 and 36 because a single amino acid change can abolish the binding ability or activity of a molecule. For example, a substitution of lysine residue by glutamic acid at position 118 of acidic fibroblast growth factor results in a substantial loss of its biological activity including the binding ability to heparin and its receptor (Burgess et al. J of Cell Bio. 111:2129-2138, 1990). Although many amino acid substitutions are possible in any given protein, the position of where such amino acid substitutions can be made is critical for maintaining the function of a protein; i.e. only certain positions can tolerate conservative substitutions without changing the relationship of three dimensional structure and function of the protein (col 2, p. 1306, Bowie et al. Science, 1990, 247:1306-1310). Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would not immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active because conformation is dependent upon surrounding residues; i.e. substitution of non-essential residues can often destroy activity. The predictive data always need to be validated by actual analyses in cells (see p. 445, the third column, second paragraph, Pawson et al. 2003, Science 300:445-452).

Moreover, the specification fails to provide sufficient guidance as to how all the polypeptides comprising fragments and variants with at least 65% identity to a fragment of SEQ ID NO:1 are related to SEQ ID NO:3 or 36 that can be used as an diagnostic

marker of heart failure. The specification only discloses that an upregulated expression level of SEQ ID NO:3 and 36 is found in heart tissue from heart failure patients but not the variant polypeptides or fragments in the disease or other diseases. It is unpredictable whether any variant polypeptides or fragments derived from SEQ ID NOs: 1, 3 and 36 would be up-regulated in patients with hear failure or other diseases. Thus, a skilled artisan cannot contemplate how to use the claimed genus of polypeptides except SEQ ID NO:3 and 36. It is also unpredictable whether all the claimed variant polypeptides or fragments are useful for a diagnostic marker of any diseases or other purposes since there is no guidance to indicate how the variant polypeptides or fragments are related to SEQ ID NO:3 or 36. It is unpredictable which, if any other variant polypeptides or fragments would be similarly upregulated, since the regulation is independent of the sequence of the protein. Since the specification fails to provide sufficient guidance as to whether the variant polypeptides or fragments would be upregulated and whether they are related to heart diseases or other diseases, a skilled artisan cannot contemplate how to use the claimed variant polypeptides.

Thus, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification and the lack of knowledge of function for each sequence, undue experimentation would be required by a skilled artisan to perform in order to practice the claimed invention as it pertains to the claimed polypeptide and the claimed composition comprising the claimed polypeptide.

6. Claims 1-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-10 and 16 are drawn to an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:3, SEQ ID NO:1, SEQ ID NO:36 or a sequence having at least 65% identity to a fragment of SEQ ID NO:1. The claims encompass a genus of polypeptides comprising structurally and functionally undefined fragments and their variants derived from SEQ ID NO:3, SEQ ID NO:1, SEQ ID NO:36 or a sequence having at least 65% identity to a fragment of SEQ ID NO:1. Applicant has not disclosed sufficient species for the broad genus of variant polypeptides or fragments related to SEQ ID NOs:1, 3 and 36. The claims do not require any particular biological activity/conserved structure/distinguishing feature. Thus, the claims encompass a genus of polypeptides that is defined only by sequence similarity. However, the instant specification fails to provide information to demonstrate Applicant's possession the

entire genus of the polypeptide variants and fragments that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of SEQ ID NOs: 3 and 36, which have a known function and activity. However, the claims are not only drawn to polypeptides having the above sequences but also to variants and fragments and polypeptides derived from SEQ ID NOs:1, 3 and 36 and variants and fragments comprising sequences having at least 65% identity to a fragment of SEQ ID NO:1. The claims only require the polypeptides to share some degree of structural similarity to SEQ ID NOs:1, 3 and 36. The specification only describes SEQ ID NOs: 3 and 36 and fails to teach the function of SEQ ID NO:1 or describe any other related proteins with limited homology. In this case, the only factor present in the claim is a partial structure in the form of a recitation of sequence similarity or percent identity. There is not even identification of any particular portion of the structure that must be conserved. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of variant and fragment polypeptides. While a generic sequence is provided, there is merely a set of common properties: there is no description of the conserved regions which are critical to the function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to

function. Structural features that could distinguish the variant and fragment polypeptides in the genus from other polypeptides are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the variant and fragment polypeptides encompassed: there is no guidance in the art as to what the defining characteristics of an isolated polypeptide with limited homology to SEQ ID NOs: 3 and 36 might be. Since the common characteristics/features of the isolated variant and fragment polypeptides are unknown, a skilled artisan can not envision the functional correlations of the genus with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The

compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claimed polypeptide and composition have not met the written description provision of 35 U.S.C. §112, first paragraph. only full length BAT3 and CGI-59 proteins, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP 2163.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by U. S. Patent No. 5948761 (Sellhamer et al., issued Sep 7, 1999).

U. S. Patent No. 5948761 (the '761 patent) teaches an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:48, which meets the limitation as recited in instant claim 1 because SEQ ID NO:48 comprises an amino acid sequence having 100% identity to an amino acid sequence of instant SEQ ID NO:3 (see the sequence alignment below; figure 8; col. 59, claims 1-12). The '761 patent also teaches a pharmaceutical composition comprising the claimed polypeptide and a pharmaceutically acceptable carrier because the polypeptide disclosed in the '761 patent is in physiological tolerable liguid, gel, diluent or excipient (see col. 17, lines 21-65). Thus, claims 1 and 16 are anticipated by US 5948761.

The sequence search results disclose as follows:

SEQ ID NO:3

```
US-08-850-910A-48
; Sequence 48, Application US/08850910A
; Patent No. 5949761
; GENERAL INFORMATION:
;   APPLICANT:  SELLHAMER, J.J.
;   APPLICANT:  LEWICKI, J.
;   APPLICANT:  SCARBOROUGH, R.M.
;   TITLE OF INVENTION:  RECOMBINANT TECHNIQUES FOR
;   TITLE OF INVENTION:  PRODUCTION OF BRAIN NATRIURETIC PEPTIDE
;   NUMBER OF SEQUENCES:  50
;   CORRESPONDENCE ADDRESS:
;     ADDRESSEE:  MORRISON & FOERSTER, LLP
;     STREET:  2000 Pennsylvania Avenue, NW, Suite 5500
;     CITY:  Washington
;     STATE:  DC
;     COUNTRY:  USA
;     ZIP:  20006-1888
;   COMPUTER READABLE FORM:
;     MEDIUM TYPE:  Diskette
;     COMPUTER:  IBM Compatible
;     OPERATING SYSTEM:  Windows
;     SOFTWARE:  FastSEQ for Windows Version 2.0b
;   CURRENT APPLICATION DATA:
;     APPLICATION NUMBER:  US/08/850,910A
;     FILING DATE:  05-MAY-1997
;     CLASSIFICATION:  435
;   PRIOR APPLICATION DATA:
;     APPLICATION NUMBER:  07/477,226
;     FILING DATE:  08-FEB-1990
;     APPLICATION NUMBER:  07/299,880
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;       FILING DATE:  19-JAN-1989
;       APPLICATION NUMBER:  07/206,470
;       FILING DATE:  14-JUN-1988
;       APPLICATION NUMBER:  07/200,383
;       FILING DATE:  31-MAY-1988
;    ATTORNEY/AGENT INFORMATION:
;       NAME:  Murashige, Kate H
;       REGISTRATION NUMBER:  29,959
;       REFERENCE/DOCKET NUMBER:  219002025212
;    TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  202-887-1500
;       TELEFAX:  202-822-0168
;       TELEX:
;  INFORMATION FOR SEQ ID NO:  48:
;    SEQUENCE CHARACTERISTICS:
;       LENGTH:  134 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:  single
;       TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-850-910A-48

  Query Match             79.6%;  Score 129;  DB 1;  Length 134;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-109;
  Matches  129;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQRNHLQGKLSELQVE 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQRNHLQGKLSELQVE 60

Qy         61 QTSLEPLQESPRPTGVWKSREVATEGIRGHRKMVLYTLRAPRSPKMVQGSGCFGRKMDRI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QTSLEPLQESPRPTGVWKSREVATEGIRGHRKMVLYTLRAPRSPKMVQGSGCFGRKMDRI 120

Qy        121 SSSSGLGCK 129
              |||||||||
Db        121 SSSSGLGCK 129
```

8. Claims 1 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by US. Patent No. 5434133 (Tanaka et al. issued Jul 18, 1995).

U. S. Patent No. 5434133 (the '133 patent) teaches an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:41, which meets the limitation as recited in instant claim 1 because SEQ ID NO:41 comprises an amino acid sequence having 100% identity to an amino acid sequence (i.e. fragment) of instant SEQ ID NO:36 (see the sequence alignment below; col. 35, claims 1-2). The '133 patent also teaches a pharmaceutical composition comprising the claimed polypeptide and a pharmaceutically acceptable carrier because the polypeptide disclosed in the '133 patent is in a pharmaceutically acceptable carrier, diluent or excipient (see col. 13, lines 18-38). Thus, claims 1 and 16 are anticipated by US 5434133.

SEQ ID NO:36

```
US-07-828-450-41
; Sequence 41, Application US/07828450
; Patent No. 5494133
; GENERAL INFORMATION:
;    APPLICANT:  TANAKA, SHOJI
;    APPLICANT:  MINAMITAKE, YOSHIHARU
;    APPLICANT:  KITAZUMA, YASUO
;    APPLICANT:  FURUYA, MAYUMI
;    APPLICANT:  MATSUO, HISAYUKI
;    TITLE OF INVENTION:  CNP ANALOG PEPTIDES AND THEIR USE
;    NUMBER OF SEQUENCES:  42
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  CUSHMAN, DARBY & CUSHMAN
;      STREET:  1625 I STREET, N.W.
;      CITY:  WASHINGTON
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20036
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/07/828,450
;      FILING DATE:  19920131
;      CLASSIFICATION:  530
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  SCOTT, WATSON T.
;      REGISTRATION NUMBER:  26,581
;      REFERENCE/DOCKET NUMBER:  9437/94133
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-861-3067
;      TELEFAX:  202-822-0944
;      TELEX:  6714627 CUSH
;  INFORMATION FOR SEQ ID NO:  41:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  32 amino acids
;      TYPE:  AMINO ACID
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-07-828-450-41

  Query Match             45.0%;  Score 27;  DB 1;  Length 32;
  Best Local Similarity   100.0%;  Pred. No. 6.8e-18;
  Matches   27;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SPKMVQGSGCFGRKMDRISSSSGLGCK 27
              |||||||||||||||||||||||||||
Db          1 SPKMVQGSGCFGRKMDRISSSSGLGCK 27
```

9. Claims 1, 3, 5, 7, 9 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by U. S. Patent No. 6812339 (Venter et al., issued Nov 2, 2004, priority Sep 8, 2000, as in IDS).

U. S. Patent No. 6812339 (the '339 patent) teaches an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:7086, which meets the limitation as recited in instant claim 1 because SEQ ID NO:7086 comprises an amino acid sequence (i.e.fragment) having at least 6 contiguous residues of SEQ ID NO:1 or having at least

65%-95 identity to a fragment of SEQ ID NO:1, which meets the limitations as recited in instant claims 1, 3, 5, 7, and 9 (see the sequence alignment below; figure 8; col. 59, claims 1-12). The '339 patent also teaches a composition comprising the claimed polypeptide in a compound or solution for diagnosis, which meets the limitation of a pharmaceutical composition comprising the claimed polypeptide and a pharmaceutically acceptable carrier as recited in instant claim 16 (see col. 33, line 3- col. 35, line 11). Thus, claims 1, 3, 5, 7, 9 and 16 are anticipated by U. S. Patent No. 6812339.

The sequence search results disclose as follows:

SEQ ID NO:1

```
US-09-949-016-7086
; Sequence 7086, Application US/09949016
; Patent No. 6812339
; GENERAL INFORMATION:
;  APPLICANT: VENTER, J. Craig et al.
;  TITLE OF INVENTION: POLYMORPHISMS IN KNOWN GENES ASSOCIATED
;  TITLE OF INVENTION:  WITH HUMAN DISEASE, METHODS OF DETECTION AND USES THEREOF
;  FILE REFERENCE: CL001307
;  CURRENT APPLICATION NUMBER: US/09/949,016
;  CURRENT FILING DATE:  2000-06-14
;  PRIOR APPLICATION NUMBER: 60/241,755
;  PRIOR FILING DATE: 2000-10-20
;  PRIOR APPLICATION NUMBER: 60/237,768
;  PRIOR FILING DATE: 2000-10-03
;  PRIOR APPLICATION NUMBER: 60/231,498
;  PRIOR FILING DATE: 2000-09-08
;  NUMBER OF SEQ ID NOS: 207012
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 7086
;   LENGTH: 706
;   TYPE: PRT
;   ORGANISM: Human
US-09-949-016-7086

  Query Match           30.4%;  Score 56;  DB 4;  Length 706;
  Best Local Similarity   76.9%;  Pred. No. 36;
  Matches   10;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          5 LPPRPPSPIPVCD 17
              |||||| | ||| |
Db        687 LPPRPPPPAPVND 699
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Conclusion

10. NO CLAIM IS ALLOWED.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

SEQ ID NO:3

```
US-09-508-435A-2
; Sequence 2, Application US/09508435A
; Patent No. 6828107
; GENERAL INFORMATION:
;  APPLICANT: Shionogi & Co., Ltd.
;  TITLE OF INVENTION: Immunoassay for BNP
;  FILE REFERENCE: 2000-125A/JJS/WMC/00177
;  CURRENT APPLICATION NUMBER: US/09/508,435A
;  CURRENT FILING DATE:  2000-03-13
;  PRIOR APPLICATION NUMBER: JP 246684/1997
;  PRIOR FILING DATE: 1997-09-11
;  NUMBER OF SEQ ID NOS: 2
;  SOFTWARE: Word (MS-DOS text)
; SEQ ID NO 2
;   LENGTH: 134
;   TYPE: PRT
;   ORGANISM: human
US-09-508-435A-2

  Query Match             79.6%;  Score 129;  DB 2;  Length 134;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-109;
  Matches  129;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVE 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVE 60

Qy         61 QTSLEPLQESPRPTGVWKSREVATEGIRGHRKMVLYTLRAPRSPKMVQGSGCFGRKMDRI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QTSLEPLQESPRPTGVWKSREVATEGIRGHRKMVLYTLRAPRSPKMVQGSGCFGRKMDRI 120

Qy        121 SSSSGLGCK 129
              |||||||||
Db        121 SSSSGLGCK 129

US-09-902-517-48
; Sequence 48, Application US/09902517
; Patent No. 6897030
; GENERAL INFORMATION:
;  APPLICANT: Seilhamer, Jeffrey J.
;  APPLICANT:  Lewicki, John
;  APPLICANT:  Scarborough, Robert M.
;  APPLICANT:  Porter, Gordon J.
;  TITLE OF INVENTION: IMMUNOASSAYS FOR HUMAN AND CANINE BRAIN
;  TITLE OF INVENTION:  NATRIURETIC PEPTIDE
;  FILE REFERENCE: 219002025213
;  CURRENT APPLICATION NUMBER: US/09/902,517
;  CURRENT FILING DATE:  2001-07-09
;  PRIOR APPLICATION NUMBER: 09/287,892
;  PRIOR FILING DATE: 1999-04-07
;  PRIOR APPLICATION NUMBER: 08/850,910
;  PRIOR FILING DATE: 1997-05-05
;  PRIOR APPLICATION NUMBER: 07/477,226
;  PRIOR FILING DATE: 1990-02-08
;  PRIOR APPLICATION NUMBER: 07/299,880
;  PRIOR FILING DATE: 1989-01-19
;  PRIOR APPLICATION NUMBER: 07/206,470
;  PRIOR FILING DATE: 1988-06-14
;  PRIOR APPLICATION NUMBER: 07/200,383
;  PRIOR FILING DATE: 1988-05-31
;  NUMBER OF SEQ ID NOS: 50
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 48
;   LENGTH: 134
;   TYPE: PRT
;   ORGANISM: Unknown
;   FEATURE:
;   OTHER INFORMATION: Comparison sequence of the prepro forms of the
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;   OTHER INFORMATION: human proteins of the invention
US-09-902-537-48

  Query Match             79.6%;  Score 129;  DB 2;  Length 134;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-109;
  Matches  129;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVE 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVE 60

Qy         61 QTSLEPLQESPAPTGVWKSREVATEGIRGHRKMVLYTLRAPASPKMVQGSGCFGRKMDRI 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QTSLEPLQESPAPTGVWKSREVATEGIRGHRKMVLYTLRAPASPKMVQGSGCFGRKMDRI 120

Qy        121 SSSSGLGCK 129
              |||||||||
Db        121 SSSSGLGCK 129


US-10-402-021-48
; Sequence 48, Application US/10402021
; Patent No. 6974861
; GENERAL INFORMATION:
;  APPLICANT: Seilhamer, Jeffrey J.
;  APPLICANT:  Lewicki, John
;  APPLICANT:  Scarborough, Robert M.
;  APPLICANT:  Porter, Gordon J.
;  TITLE OF INVENTION: PHARMACEUTICAL COMPOSITIONS AND METHODS USING NATRIURETIC PEPTIDES
;  TITLE OF INVENTION:  (AMENDED)
;  FILE REFERENCE: 219002025203
;  CURRENT APPLICATION NUMBER: US/10/402,021
;  CURRENT FILING DATE:  2003-03-27
;  PRIOR APPLICATION NUMBER: 09/287,892
;  PRIOR FILING DATE: 1999-04-07
;  PRIOR APPLICATION NUMBER: 08/850,910
;  PRIOR FILING DATE: 1997-05-05
;  PRIOR APPLICATION NUMBER: 07/477,226
;  PRIOR FILING DATE: 1990-02-08
;  PRIOR APPLICATION NUMBER: 07/299,880
;  PRIOR FILING DATE: 1989-01-19
;  PRIOR APPLICATION NUMBER: 07/206,470
;  PRIOR FILING DATE: 1988-06-14
;  PRIOR APPLICATION NUMBER: 07/200,383
;  PRIOR FILING DATE: 1988-05-31
;  NUMBER OF SEQ ID NOS: 50
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 48
;  LENGTH: 134
;  TYPE: PRT
;  ORGANISM: Unknown
;  FEATURE:
;  OTHER INFORMATION: Comparison sequence of the prepro forms of the
;  OTHER INFORMATION: human proteins of the invention
US-10-402-021-48

  Query Match             79.6%;  Score 129;  DB 2;  Length 134;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-109;
  Matches  129;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVE 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MDPQTAPSRALLLLFLHLAFLGGRSHPLGSPGSASDLETSGLQEQRNHLQGKLSELQVE 60

Qy         61 QTSLEPLQESPAPTGVWKSREVATEGIRGHRKMVLYTLRAPASPKMVQGSGCFGRKMDRI 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QTSLEPLQESPAPTGVWKSREVATEGIRGHRKMVLYTLRAPASPKMVQGSGCFGRKMDRI 120

Qy        121 SSSSGLGCK 129
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Db        121 SSSSGLGCK 129
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SEQ ID NO:36

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US-08-297-330-2
; Sequence 2, Application US/08297330
; Patent No. 5983108
;  GENERAL INFORMATION:
;    APPLICANT:  Wei, Chi-Ming
;    APPLICANT:  Burnett, John C.
;    TITLE OF INVENTION:  Vasonatrin Peptide and Analogs
```

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;    TITLE OF INVENTION:  Thereof
;    NUMBER OF SEQUENCES:  17
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Merchant & Gould
;      STREET:  3100 No. 5583108west Center
;      CITY:  Minneapolis
;      STATE:  MN
;      COUNTRY:  USA
;      ZIP:  55402-4131
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/297,330
;      FILING DATE:
;      CLASSIFICATION:  514
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/025,935
;      FILING DATE:  03-MAR-1993
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Woessner, Warren D.
;      REGISTRATION NUMBER:  30,440
;      REFERENCE/DOCKET NUMBER:  1016.99-US01
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  612-332-5300
;      TELEFAX:  612-332-9081
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  32 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
;    ORIGINAL SOURCE:
;      ORGANISM:  Mature human brain natriuretic peptide
;      ORGANISM:
US-08-297-930-2

  Query Match              45.0%;  Score 27;  DB 1;  Length 32;
  Best Local Similarity   100.0%;  Pred. No. 6.8e-18;
  Matches   27;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SPKMVQGSGCFGRKMDRISSSSGLGCK 27
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Db          1 SPKMVQGSGCFGRKMDRISSSSGLGCK 27


US-08-451-240-22
; Sequence 22, Application US/08451240
; Patent No. 5665706
; GENERAL INFORMATION:
;    APPLICANT:  Lowe, David
;    APPLICANT:  Cunningham, Brian
;    APPLICANT:  Oare, David
;    APPLICANT:  McDowell, Robert S.
;    APPLICANT:  Burnier, John
;    TITLE OF INVENTION:  RECEPTOR SPECIFIC ATRIAL NATRIURETIC
;    TITLE OF INVENTION:  PEPTIDES
;    NUMBER OF SEQUENCES:  47
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Genentech, Inc.
;      STREET:  460 Point San Bruno Blvd
;      CITY:  South San Francisco
;      STATE:  California
;      COUNTRY:  USA
;      ZIP:  94080
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  5.25 inch, 360 Kb floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  patin (Genentech)
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/451,240
;      FILING DATE:
;      CLASSIFICATION:  530
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/362552
;      FILING DATE:  06-JAN-1995
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/152994
;      FILING DATE:  12-NOV-1993
```

```
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Kubiney, Jeffrey S.
;      REGISTRATION NUMBER:  36,575
;      REFERENCE/DOCKET NUMBER:  P0844P1C1
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  415/227-8228
;      TELEFAX:  415/952-9881
;      TELEX:  910/371-7168
;  INFORMATION FOR SEQ ID NO:  22:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  32 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
US-08-451-240-22

  Query Match             45.0%;  Score 27;  DB 1;  Length 32;
  Best Local Similarity   100.0%;  Pred. No. 6.8e-18;
  Matches   27;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SPKMVQGSGCFGRKMDRISSSSGLGCK 27
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Db          1 SPKMVQGSGCFGRKMDRISSSSGLGCK 27
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SEQ ID NO:1

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US-10-437-963-107995
; Sequence 107995, Application US/10437963
; Publication No. US20040123343A1
; GENERAL INFORMATION:
;  APPLICANT:  La Rosa, Thomas J.
;  APPLICANT:  Kovalic, David K.
;  APPLICANT:  Zhou, Yihua
;  APPLICANT:  Cao, Yongwei
;  APPLICANT:  Wu, Wei
;  APPLICANT:  Boukharov, Andrey A.
;  APPLICANT:  Barbazuk, Brad
;  APPLICANT:  Li, Ping
;  TITLE OF INVENTION: Rice Nucleic Acid Molecules and Other Molecules Associated With
;  TITLE OF INVENTION:  Plants and Uses Thereof for Plant Improvement
;  FILE REFERENCE: 38-21(53221)B
;  CURRENT APPLICATION NUMBER: US/10/437,963
;  CURRENT FILING DATE:  2003-05-14
;  NUMBER OF SEQ ID NOS: 204966
; SEQ ID NO 107995
;   LENGTH: 86
;   TYPE: PRT
;   ORGANISM: Oryza sativa
;   FEATURE:
;   OTHER INFORMATION: Clone ID: PAT_MRT4530_12292C.1.pep
US-10-437-963-107995

  Query Match             27.3%;  Score 9;  DB 4;  Length 86;
  Best Local Similarity   100.0%;  Pred. No. 1.1;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          6 PPRPPSPIP 14
              |||||||||
Db          3 PPRPPSPIP 11

US-10-703-032-191813
; Sequence 191813, Application US/10703032
; Patent No. 7214786
; GENERAL INFORMATION:
;  APPLICANT:  Kovalic, David K.
;  APPLICANT:  Andersen, Scott E.
;  APPLICANT:  Byrum, Joseph R.
;  APPLICANT:  Conner, Timothy W.
;  APPLICANT:  Cao, Yongwei
;  APPLICANT:  Masuoni, James D.
;  APPLICANT:  Zhou, Yihua
;  TITLE OF INVENTION: Nucleic Acid Molecules And Other Molecules Associated With
;  TITLE OF INVENTION:  Plants
;  FILE REFERENCE: 38-21(53374)B
;  CURRENT APPLICATION NUMBER: US/10/703,032
;  CURRENT FILING DATE:  2003-11-06
;  PRIOR APPLICATION NUMBER: 10/020,338
;  PRIOR FILING DATE: 2001-12-12
;  NUMBER OF SEQ ID NOS: 211164
; SEQ ID NO 191813
;   LENGTH: 98
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;   TYPE: PRT
;   ORGANISM: Triticum aestivum
;   FEATURE:
;   NAME/KEY: unsure
;   LOCATION: (1)..(98)
;   OTHER INFORMATION: unsure at all Xaa locations
;   FEATURE:
;   OTHER INFORMATION: Clone ID: PAT_TA_86231.pep
US-10-703-032-19813

  Query Match          27.3%;  Score 9;  DB 3;  Length 98;
  Best Local Similarity   100.0%;  Pred. No. 0.24;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          4 PLPPRPPSP 12
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Db         74 PLPPRPPSP 82
```

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
August 25, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647